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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,782	07/09/2001	Susan Hardin	0007/01UTL	9388

23873 7590 01/21/2003

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EXAMINER

SMITH, CAROLYN L

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 01/21/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/901,782

Applicant(s)

HARDIN ET AL.

Examiner

Carolyn L Smith

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 25-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☒ Claim(s) 16 is/are objected to.
- 8) ☒ Claim(s) 1-34 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>11,12</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants elections with traverse of Group I (claims 1-24) and species A (a polymerizing agent which is a polymerase) and subspecies A (a polymerase which is a *Taq* DNA polymerase I) in Paper No. 14, filed 11/18/02, are acknowledged. Claims 25-34 are withdrawn from consideration as being drawn to non-elected Groups.

Applicants' traversal is on the grounds that Groups I, V, and VI are related in that the methods of Groups V and VI are based on the use of Group I and that restricting between them would not speed examination and would not result in a duplication of effort.

The applicants' request to combine Groups I, V, and VI into one invention was found unpersuasive because of the following reasons (summarized from the restriction paper):

Inventions in Groups I, V, and VI are related as product and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP §806.05(h)). In the instant case the composition of Group I may be utilized in distinct usages as needed in Group V in a system and method for determining molecular sequence information, in a method of sequencing an individual nucleic acid molecule or numerous individual molecules in parallel as in Group VI, or alternatively, in cell growth inhibition studies. All of these usages are distinct as requiring distinct and different functions thereof without overlapping search due to different subject matter. This lack of overlapping searches documents the undue search burden if they were searched together.

The requirements are still deemed proper and are therefore made FINAL.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821 (a)(1) and (a)(2). See for example, pages 64-67 in the specification; Figures 5, 10, and 11; and elsewhere. However, this application fails to comply with the requirements of 37 CFR § 1.821 through 1.825, because it lacks SEQ ID Nos cited along with each sequence in the specification or Figures. Applicants are also reminded that SEQ ID Nos are not required in Figures per se, however, the corresponding SEQ ID Nos then are required in the Brief Description of the Drawings section in the specification. Applicant(s) are required to submit a new computer readable form sequence listing, a paper copy, or CD-ROM for the specification, statements under 37 CFR § 1.821 (f) and (g). Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office Action.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to real-time sequence determination whereas in contrast the elected claims include a *Taq* DNA polymerase I.

Claims herein under examination are 1-24.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the declaration contains an incorrect date for the priority document which is the provisional parent application.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 5, line 3, and elsewhere. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the following informality: “att,achment” on page 37, line 12 and “Mutagensis” on page 64, line 16, are misspelled. Appropriate correction of these and any other misspellings or grammatical errors is required.

Claim Objections

Claim 16 is objected to because of the following informality: “comprise” on line 1 should end in an “s.” Appropriate correction is required.

Claims Rejected Under 35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 6, 19, and 24 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 6, 19, and 24 recite attachment site numbers ("513-518, 643, 647, 649, and 653-661") on *Taq* DNA polymerase I; however, no sequence is disclosed for *Taq* DNA polymerase I by which to determine where these sites are therein. This enzyme is noted in a reference cited on page 39, lines 5-8 of the specification, but this is essential subject matter which cannot be properly enabled by reference to a printed publication. The incorporation of essential material in

the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1-4, 7-8, 10-14, 18, and 20-22 and the dependent claims therefrom contain embodiments which are beyond the elected invention, particularly “polymerizing agent” and “polymerase.” Correction is suggested by stating only the embodiments (in this case, “*Taq* DNA polymerase I”) which are part of the invention.

Claims 1 (line 2), 7 (line 2), and 20 (line 2) recite the phrase “located at or near” which is vague and indefinite. It is unclear what degree of closeness qualifies as being “near”. Clarification of the metes and bounds of the claims via clearer claim wording is required.

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Claims 1, 7, and 20 are rejected along with claims 2-6, 8-9, and 21-24 due to their direct or indirect dependence therefrom.

Claims 1 (line 2), 7 (line 2), 10 (line 2), and 20 (line 2) recite the phrase “associated with” which is vague and indefinite. It is unclear what parameters are used and to what degree in order to determine that the tag is “associated with” the polymerizing agent. It is also unclear if the association is in relation to the “site” as mentioned or to the polymerizing agent as a whole. Claims 1, 7, 10, and 20 are rejected along with claims 2-6, 8-9, 11-19, and 21-24 due to their direct or indirect dependence therefrom.

Claims 6 (line 3), 19 (line 3), and 24 (line 3) recite the phrase “mixtures or combinations thereof of the *Taq* polymerase” which is vague and indefinite. It is unclear what else may be included in these multiple entities besides *Taq* DNA polymerase I. Clarification of the metes and bounds of these claims via clearer claim wording is required.

Claim 16 is vague and indefinite due to the unclarity of citing an abbreviation, such as dNTP on line 1. Correction is suggested by amending in of the full name in parentheses. Claim 18 is also rejected due to its dependency from claim 16.

Claim 16, line 2, recites the term “group” which is vague and indefinite. It is unclear which entity the “group” is a part of, the polymerase, the monomer, or the dNTP. Clarification of the location of the “group” is required. Claim 18 is also rejected due to its dependency from claim 16.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 7-18, and 20-23 are rejected under 35 U.S.C. 102(a) and (b) as being anticipated by Williams (WO 00/36151) and Brandis (1999), respectively.

Williams discloses a *Taq* DNA polymerase (p. 8, lines 23-28) in which a fluorescently labeled dNTP (tag) is associated with the polymerase during monomer incorporation (p. 8, lines 1-9). The tag consists of a labeled nucleotide triphosphate (NTP) having a γ -phosphate with a fluorophore moiety attached and a quencher moiety that sufficiently prevents fluorescence until incorporation of the NTP at which time the γ -phosphate with the fluorophore moiety is released and detected (p. 8, lines 10-20). Williams discloses the fluorescence is detected when labeled dNTPs are incorporated into the strand and fluorescence is induced (p. 9, lines 28-29). Williams discloses that upon incorporation, the fluorescent dye molecule is released with pyrophosphate from the polymerase and then swept away from the parent DNA molecule by the flow (p. 10, lines 13-17), suggesting the polymerase's detectable property reverts back to its initial state. Williams discloses that as the polymerase moves along the DNA, the nucleotide sequence is read from the order of released dyes (p. 14, lines 30-31). Williams discloses the possible presence of

other polymerases, such as HIV reverse transcriptase, as stated in claims 5, 9, and 23. Thus, Williams anticipates the limitations in claims 1-5, 7-10, 17, and 20-23.

A 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra references are cited to show that a characteristic not disclosed in the reference is inherent (see MPEP 2131.01 (c)). Brandis discloses a *Taq* DNA polymerase I including an inherent characteristic that polymerases go through conformational changes (abstract). Brandis also discloses that a change occurs in a fluorescent label during the change in conformational states of the polymerase when nucleotide binding occurs as the polymerase is active (abstract). Thus, Brandis further anticipates claims 11-18 of the instant invention.

Claims 1, 3, and 4 are rejected under 35 U.S.C. 102(e)(2) as being anticipated by Patel et al. (P/N 6,329,178).

Patel et al. disclose the *Taq* DNA polymerase I (col. 13, lines 5-8) active site is highly mutable and can accommodate many amino acid substitutions without significantly affecting activity (col. 2, lines 63-66). Patel et al. disclose that mutant DNA polymerases can incorporate unconventional nucleotides (col. 3, lines 44-48), such as bases labeled with a reporter molecule and fluorescently labeled bases (col. 6, lines 14-19) which suggests types of tags. Patel et al. disclose the fluorescently labeled tags exhibiting different emissions when a DNA fragment is extended by DNA polymerase (col. 10, lines 38-67). Thus, Patel et al. anticipate claims 1, 3, and 4.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

January 13, 2003


ARDIN H. MARSCHEL
PRIMARY EXAMINER